

### **Remarks**

The Applicants would like to thank the Examiner for a telephonic interview on May 30, 2008. The Applicants acknowledge the Examiner's comments in the Interview Summary mailed on June 4, 2008.

It is believed that the following remarks address and overcome the outstanding 103(a) rejection to the claims. Reconsideration of each of the rejections is therefore respectfully requested.

### **Rejections under 35 USC 103**

The Examiner has maintained the rejection of claims 86, 89, 94-98, 100-102 and 110-119 as being unpatentable over Rana in view of Florence, "Manoharan I", and Cook and evidenced by "Manoharan II". Applicants traverse and respectfully request reconsideration based on the following remarks.

The claimed invention recites a double-stranded ribonucleic acid (dsRNA) including a complementary RNA strand, a sense RNA strand and only one lipophilic group having a  $\log K_{ow}$  exceeding 1. The complementary RNA strand has a nucleotide sequence which is complementary to a target RNA. The target RNA is an mRNA transcript of a target gene or of a (+) strand RNA virus. The lipophilic group is either covalently attached to a 5'-end of the complementary RNA strand wherein a linkage between the lipophilic group and the 5'-end of the complementary RNA strand comprises a phosphodiester group, or the lipophilic group is covalently attached to a 5'-end of the sense RNA strand. Applicants submit that the references, both alone and when read in combination, would not render obvious the claimed invention.

Rana discloses compositions for RNA interference and related methods and further discloses modifications of the RNA at the 2' position or at the nucleobase but teaches away from the 5' modification. This is evidenced by Examples I-VII. Rana explicitly stated in Example III that the free 5' OH on the antisense strand of the siRNA duplex is required for RNA interference. The instant claims are directed to the 5' modification, thus are not obvious over Rana in view of Florence, Manoharan I and Cook and evidenced by Manoharan II. Rana demonstrates that the 5' hydroxyl determines the RNAi activity and further demonstrates that modification at the 3' has little effect (Example IV). Therefore, when reading Rana as a whole, one of ordinary skill in the art would not be motivated to modify the termini of the siRNA.

Since Florence, Manoharan I, Cook and Manoharan II depends on Rana as the primary reference and because the Applicants have already shown that Rana teaches away from the instant claimed invention, therefore the secondary references Florence, Manoharan I, Cook and Manoharan II are moot.

Because the teachings of Rana, Florence, "Manoharan I", Cook and "Manoharan II", either alone or in combination would not lead one in the art to arrive at the claimed invention the cited references do not support a *prima facie* case of obviousness. Thus, withdrawal of the rejections is respectfully requested.

### **Summary**

Applicants have amended the claims and provided arguments to address the outstanding rejection of the claims. It is believed that the rejections have been addressed and that the application is in condition for allowance.

Please apply any charges or credits to Deposit Account No 50-2762, referencing Attorney Docket Number (A2038-7052US).

Respectfully submitted,  
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